

## A ventral root avulsion injury model for neurogenic underactive bladder studies.

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<b>Authors:</b>	Huiyi H Chang, Leif A Havton
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### Public Summary:

Neurological conditions can cause bladder problems. A common bladder problem is referred to as an underactive bladder. In this condition, the bladder is unable to empty normally because the bladder contractions are weak. The causes of an underactive bladder can be many and reflect different diseases and conditions. An important cause for underactive bladders is nerve injuries, especially injuries that result in a disconnection between peripheral nerves and the bladder wall. In such situations, the bladder does not fully empty and there is a residual volume of urine after attempts to empty the bladder. Many people with this type of bladder problem need to use bladder catheters to empty the bladder. There are no known or successful treatments for underactive bladders. In this review article, we are discussing several experimental studies that have characterized animal models for the study of underactive bladders. Such models are important, as they may help explain causes and mechanisms for underactive bladder as well as identify potential new treatments and interventions. We describe, in part, a nerve root injury model that separates lower nerve roots from the spinal cord with the effect of causing a disconnect between the spinal cord and bladder. This laboratory model has several components in common with the human condition and has also been successfully translated to larger animal models. Specifically, both the laboratory model and the human condition include loss of reflexes and a decreased ability to empty the bladder voluntarily. When the nerve root lesion is performed on both the left and right sides of the spinal cord, there is a more pronounced effect with more severe bladder dysfunction. Interestingly, when the injured nerve roots are surgically reattached to the spinal cord to allow for nerve regeneration to occur from the spinal cord to the peripheral organs in the pelvis, there is improvement in bladder function. This surgical approach for nerve root repair may have translational research implications.

### Scientific Abstract:

Detrusor underactivity (DU) is defined as a contraction of reduced strength and/or duration during bladder emptying and results in incomplete and prolonged bladder emptying. The clinical diagnosis of DU is challenging when present alone or in association with other bladder conditions such as detrusor overactivity, urinary retention, detrusor hyperactivity with impaired contractility, aging, and neurological injuries. Several etiologies may be responsible for DU or the development of an underactive bladder (UAB), but the pathobiology of DU or UAB is not well understood. Therefore, new clinically relevant and interpretable models for studies of UAB are much needed in order to make progress towards new treatments and preventative strategies. Here, we review a neuropathic cause of DU in the form of traumatic injuries to the cauda equina (CE) and conus medullaris (CM) portions of the spinal cord. Lumbosacral ventral root avulsion (VRA) injury models in rats mimic the clinical phenotype of CM/CE injuries. Bilateral VRA injuries result in bladder areflexia, whereas a unilateral lesion results in partial impairment of lower urinary tract and visceromotor reflexes. Surgical re-implantation of avulsed ventral roots into the spinal cord and pharmacological strategies can augment micturition reflexes. The translational research need for the development of a large animal model for UAB studies is also presented, and early studies of lumbosacral VRA injuries in rhesus macaques are discussed.